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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/295,463	04/13/1999	LEX M. COWSERT	ISIS-3455	7206
35807	7590	05/23/2005	EXAMINER	
FENWICK & WEST LLP 801 CALIFORNIA STREET MOUNTAIN VIEW, CA 94014			MORAN, MARJORIE A	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 05/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/295,463	Applicant(s) COWSERT ET AL.	
	Examiner Marjorie A. Moran	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 February 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 55,56,58-72,74-76,78-83,85-87 and 99-102 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 55,56,58-72,74-76,78-83,85-87 and 99-102 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

S. O. O.

Continued Examination Under 37 CFR 1.114

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Applicant is advised that the examiner for this application has changed. Claims 55, 56, 58-72, 74-76, 78-83, 85-87, and 99-102 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 55, 56, 58-72, 74-76, 78-83, 85-87, and 99-102 are again rejected, as previously set forth in the office action of 6/9/04 and further elucidated in the Advisory Action of 12/9/04, under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Applicant's arguments filed 2/14/05 have been fully considered but they are not persuasive. In response to the argument that Figures 4-6 provide support for the combination of a thermodynamic properties and at least one other criterion in a step of generating in silico compounds, it is noted that a step of generating oligonucleotide sequences is performed BEFORE any step of calculating thermodynamic properties or scores, thus there is no support in the Figures for generating an in silico compound of any kind "according to" a thermodynamic property, whether in combination with another a property or alone. The method disclosed in the Figures is one wherein a list of PREVIOUSLY GENERATED compounds is selected based on various properties. This is not reflected in the steps of the rejected claims. Further, and as previously set forth, the assessment of a compound for a criterion such as hybridization (targeting) is performed separately from the thermodynamic property calculations. Figures 5 and 6 present these steps as being separate, with no overlapping or connecting elements which would lead one skilled in the art to interpret them as being preformed in

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combination, as embodied by the limitations of the pending claims. In response to the argument that pages 19-24 of the originally filed specification provide support for the limitations in question, it is noted that page 19, lines 16-18 discloses that FOLLOWING calculation of thermodynamic properties, desired sequence properties to be scored are selected. The disclosure of pages 19-24 contains references to the Figures. Again, it is noted that all "scoring" is preformed as a selection step AFTER generation of virtual oligonucleotides, and is not performed as part of the generation step itself. Further, and as set forth in previous office actions, the criteria listed in the claims for combination with thermodynamic properties do not coincide with the "sequence properties" or "homology" calculations disclosed by the specification and Figures as being scored following the thermodynamic calculations.

For these reasons and those previously set forth, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 55, 56, 58-72, 74-76, 78-83, 85-87, and 99-102 are again rejected under 35 U.S.C. 103(a) as being unpatentable over AGRAFIOTIS et al. (5,463,564) in view of UHLMANN et al. (1990), DOWER et al. (5,639,603), and HAFF et al. (5,720,923) or HARRIS et al. (5,650,122).

Applicant's arguments filed 2/14/05 have been fully considered but they are not persuasive. In response to the argument that the prior art does not teach the claimed combination of a thermodynamic property in combination with at least one other criterion selected from targeting to functional regions..., it is noted that AGRAFIOTIS teaches analysis of physical and/or electronic property data related to his generated compounds (col. 11, lines 57-65 and col. 12, lines 10-47). AGRAFIOTIS also teaches that his synthesis generator uses a combination of data including structural, electronic and physiochemical, and receptor fit criteria (col. 16, line 60-col. 17, line 2), thus teaching a combination of thermodynamic and other criteria, and suggesting "targeting" to a functional region (e.g. receptor) as one of his other criteria. As at least UHLMANN and DOWER teach targeting to and/or synthesis of nucleic acids, the examiner maintains that the combination of references teaches all of the claimed limitations and makes obvious the claimed methods. For these reasons and those previously set forth, the rejection is maintained.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571) 272-0720. The examiner can normally be reached on Mon,Wed: 7-1:30; Tue,Thur: 7:30-6; Fri 7-3:30 EST.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marjorie A. Moran
Primary Examiner
Art Unit 1631

Marjorie A. Moran
5/16/05